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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/055,145	04/03/1998	DONALD P. WEEKS	3553-18	3535

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EXAMINER

KRUSE, DAVID H

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/055,145

Applicant(s)

WEEKS ET AL.

Examiner

David H. Kruse

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2004 and 18 January 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,5-7,21-24,36-39,44,47,48,50-58,60-62,64,65,68,72 and 73 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,5,7,21,24,36,39,44,47,48,50-56,60-62,64,65 and 68 is/are rejected.
- 7) ☒ Claim(s) 3,6,22,23,28,37,38,53,57,72 and 73 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 8/8/2004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

STATUS OF THE APPLICATION

1. This Office action is in response to the Amendment and Remarks filed 2 December 2004 and 18 January 2005.
2. Applicant's statements concerning the 5 January 2005 personal interview in the response filed 18 January 2005 are noted.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

4. Claims 2, 5, 7, 21, 24, 36, 39, 44, 47, 48, 50-56, 60-62, 64, 65 and 68 are and remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The first issue is Applicant's amendments to claims 2, 5, 21, 36, 52, 56, 58 and 62 to include the limitations "wherein said oxygenase comprises an iron-sulfur cluster" and "wherein said oxygenase binds free Fe²⁺". The Examiner has reviewed the specification and does not find sufficient written description support for these limitations. It is the Examiner's opinion that said limitations constitute entry of New Matter into the claims. Applicant asserts that support for the limitation "wherein said oxygenase binds free Fe²⁺" can be found on page 52, lines 15-18 of the specification (page 8 of the Response filed 18 January 2005). This section of the specification is not found to be

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sufficient to support such an amendment. The specification only describes the free iron requirement of the ferredoxin component of the enzyme complex on pages 48-50 of the specification, but is silent concerning any iron requirement by the oxygenase component of the enzyme complex. Applicant argues that there was a substantial amount of art-recognized correlation and relationship between the structure of Rieske non-heme iron-binding oxygenases that transfer electrons through iron-sulfur clusters and free iron atoms and the function of these enzymes (page 9, 2nd paragraph of the Remarks filed 18 January 2005). The Examiner has reviewed the teachings of Mason *et al* 1992, which Applicant asserts teaches these correlations. Mason *et al* 1992 states that the iron binding site is the least well understood component and that any discussion of its structure and function will necessarily be speculative (paragraph spanning pages 293-294). Mason *et al* 1992 states that "If the iron represents the site at which O₂ reacts, it is presumed to be close to the substrate-binding site" but also says the mechanism of the dioxygenase reaction remains to be elucidated (page 294). Mason *et al* 1992 further states that apparently two or possibly three classes of proteins contain Rieske-type [2Fe-2S] clusters (page 298). Hence, such a free iron binding sites does not inherently describe a structural-functional relationship of a dicamba-degrading oxygenase. Applicant argues that it was known in the art at the time of the invention that the binding site for free iron is situated in immediate proximity to the portion of the substrate that is modified in the chemical reaction catalyzed by the oxygenase_{DIC}. This argument is addressed above.

The amendments to claims 2, 5, 21, 36, 52, 56, 58 and 62 as discussed above narrow the scope of the claimed invention. Such a narrowing is viewed by the Examiner as introducing New Matter into the claims in view of *Purdue Pharma L.P. v. Faulding Inc.*, 56 USPQ2d 1481 (CA FC 2000). In *Purdue Pharma L.P.*, the court taught that in the case of the '360 patent, there was nothing in the written description that would suggest to one skilled in the art that the claimed ratio is an important defining quality of the formulation, nor did the disclosure motivate one to calculate the ration (at 1486). In the instant application, Applicant's specification does not motivate one of skill in the art to exclude other oxygenases and only look to those of a specific subgenus.

Claims 2, 5, 7, 21, 24, 36, 39, 44, 47, 48, 50-56, 60-62, 64, 65 and 68 remain rejected as lacking adequate written description for the reasons of record in the Office Action mailed on 28 May 2005. Applicant's arguments filed 2 December 2004 and 18 January 2005 have been fully considered but are not found to be persuasive.

The instant claims are directed to isolated DNA molecules encoding a dicamba degrading oxygenase that is at least about 65% or 85% identical to that described in SEQ ID NO: 4, wherein Applicant only describe a single species of the claimed genus.

Applicant's referral to Figure A of the Weeks December 2002 Declaration does not appear to be pertinent to the instant rejection because such a Declaration containing a Figure A is not of record.

Applicant argues that the structure for the iron-sulfur cluster and mononuclear non-heme iron binding site were recognized in the art at the time of the invention for a variety of oxygenases, and particularly includes the vanillate demethylase which is the

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oxygenase to which the claimed dicamba-degrading oxygenase is most homologous (page 10, 3rd paragraph of the Remarks filed 18 January 2005). Applicant argues that the presently claimed oxygenase is clearly described and identified both structurally and functionally as a member of the genus of dicamba-degrading oxygenases having 65% identity to SEQ ID NO: 4 (page 10, 4th paragraph of the Remarks filed 18 January 2005). Applicant argues that one of skill in the art can readily identify the iron-sulfur cluster structure in SEQ ID IN: 4 and therefore avoid modifications to this site that would be predicted to disrupt functionality of the enzyme (page 11, 1st paragraph of the Remarks filed 18 January 2005). Applicant argues that one of skill in the art can readily identify what portion of the oxygenase structure lie in proximity to the free iron binding site and also avoid modifications to the region of the structure that would be predicted to disrupt functionality (page 11, 2nd paragraph of the Remarks). These arguments are not found to be persuasive because Applicant does not provide the guidance on what structural features are critical to the coding sequence of the claimed DNA encoding a dicamba-degrading oxygenase as broadly claimed. As discussed supra, the art states that Rieske-type [2Fe-2S] clusters are a structural feature of a several classes of proteins and that the relationship of the free iron binding sites and the function of the enzyme is at best speculative.

Applicant argues that the amino acids in the substrate binding region that account for the dicamba-binding specificity will be expected to be very few, since structures bound by different oxygenases are quite similar and that other surrounding amino acids often can be changed without significantly affecting the ability of the

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enzyme to bind the substrate and to catalyze the usual reaction involving the substrate (page 12 of the Remarks filed 18 January 2005). This argument is not found to be persuasive because as previously stated by the Examiner, Applicant does not describe what structural feature of a dicamba-degrading oxygenase is associated with the function.

5. Claims 2, 5, 7, 21, 24, 36, 39, 44, 47, 48, 50-56, 60-62, 64, 65 and 68 remain rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the DNA molecule of SEQ ID NO: 3, DNA molecules encoding the dicamba-degrading oxygenase of SEQ ID NO: 4, methods of using said DNA molecules and plants comprising said molecules, does not reasonably provide enablement for any DNA molecule encoding a dicamba-degrading oxygenase within the scope of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record in the Office Action mailed on 28 May 2005. Applicant's arguments filed 2 December 2004 and 18 January 2005 have been fully considered but are not found to be persuasive. Applicant's arguments filed 18 January 2005 have been substantially addressed above.

Applicant's arguments directed to the distinction between the dicamba-degrading oxygenase of the instant invention and cytochrome P450 oxygenases that use a heme groups to transfer electrons is noted as is found to be persuasive to the extent that it relates to the teachings of the art concerning cytochrome P450 oxygenases (page 16,

2nd paragraph of the Remarks filed 2 December 2004). The argument is not found to be fully persuasive because Applicant's own specification teaches that the dicamba-degrading oxygenase has a requirement for a reductase and thus the issue of structural feature is relevant to the instant rejection.

Applicants argue that it was known at the time of the invention that the binding site for free iron in a Rieske non-heme iron-binding oxygenase is situated in immediate proximity to the portion of the substrate that is modified in the chemical reaction catalyzed by the oxygenase (page 16, 2nd paragraph of the Remarks filed 2 December 2004). This argument has been addressed supra.

Applicant argues that one of skill in the art would clearly be able to modify up to 35% of the protein sequence without undue experimentation while predictably maintaining protein function, and that the specification provides assays by which dicamba-degrading catalytic activity can easily be evaluated. Applicant argues that the post-filing data have demonstrated that one of skill in the art can easily produce mutations that do not disrupt protein function (page 17, 1st paragraph of the Remarks filed 2 December 2004). This argument is not found to be persuasive because Applicant provides no guidance on what 35% of the structure can be modified without affecting function, in addition the evidence of record does not support the breadth of the claims.

Applicants argue that they have established that, as predicted by the specification, one can use the sequence for the oxygenase of the present invention and readily identify, isolate and clone additional dicamba-degrading oxygenases that fall

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within the scope of Claim 2 and that the fact that the identified dicamba-degrading oxygenases from other bacteria are greater than 90% identical to SEQ ID NO:4 does not discount their value in demonstrating the ease in obtaining an oxygenase within the scope of Claim 2 (page 17 of the Remarks filed 2 December 2004). This argument is not found to be persuasive because Applicant did not provide evidence of sequence identity of other dicamba-degrading oxygenases, and such evidence does not support the breadth of the instant claims.

Applicant's argument directed to biologically active fragments of SEQ ID NO: 4 in the Remarks filed 2 December 2004 are moot in view of the amendment filed 18 January 2005 (see page 17, 3rd paragraph of the Remarks filed 2 December 2004).

Allowable Subject Matter

6. Claims 3, 6, 22, 23, 37, 38, 53, 57, 72 and 73 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-0547.

DAVID H. KRUSE, PH.D.
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read "David H. Kruse", written in a cursive style.

David H. Kruse, Ph.D.
30 March 2005

10. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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